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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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MAYER & WILLIAMS PC
251 NORTH AVENUE WEST
2ND FLOOR
WESTFIELD, NJ 07090

EXAMINER	
RAE, CHARLESWORTH E	

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1611	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/667,151	ZHONG ET AL.	
	Examiner	Art Unit	
	CHARLESWORTH RAE	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12/01/08*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-39* is/are pending in the application.

4a) Of the above claim(s) *22-37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21, and 38-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This is a non-final action. The finality of the previous Office action is hereby withdrawn pursuant to 37 CFR 1.129(a). Applicant's submission after final filed on 12/01/08 has been entered.

In view of the Appeal Brief filed on 03/02/09, PROSECUTION IS HEREBY REOPENED.

To avoid abandonment of the application, appellant must exercise one of the following two options:

(1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(2) initiate a new appeal by filing a notice of appeal under 37 CFR 41.31 followed by an appeal brief under 37 CFR 41.37. The previously paid notice of appeal fee and appeal brief fee can be applied to the new appeal. If, however, the appeal fees set forth in 37 CFR 41.20 have been increased since they were previously paid, then appellant must pay the difference between the increased fees and the amount previously paid.

A Supervisory Patent Examiner (SPE) has approved of reopening prosecution by signing below.

Status of the Claims

Claims 1-36 are currently pending in this application.

Claims 22-37 are withdrawn for being directed to non-elected subject matter.

Claims 1-21, and 38-39 are under examination.

Response to applicant's arguments

Nonstatutory Obviousness-Type Double-Patenting

This rejection is withdrawn in view of the restriction requirement imposed in co-pending US Application No. 11/124,828/(Pub. No. 2006/0251581 A1), wherein reference claim 40 (directed to a product) has been withdrawn. It is noted that this rejection may be reinstated if reference claim 40 is rejoined.

REJECTIONS

Claim rejections – 35 USC 103(a)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-6, 11-12, 20-21 are rejected under 103(a) as being unpatentable over Escandon et al. (US Patent Application Pub. No. 2003/0092689; already made of record).

Escandon et al. (US Patent Application Pub. No. 2003/0092689) teach a method of chemically ablating prostate tissue comprising injecting an effective amount ethanol or an injectable gel comprising ethanol into prostate tissue (paras. 0031-0037; see also reference claim 6), wherein the ethanol is medical-grade ethanol (also known as anhydrous alcohol, absolute alcohol, or absolute ethyl alcohol; para. 0061). Escandon et al. state that the **ablating action of the ethanol is due to several processes, including dehydration of cells, coagulation of proteins, and thrombosis of vessels that feed the tissue** (para. 0044, last three lines). Escandon et al. disclose that chemical ablation may be achieved, for example, by direct injection of a chemoblation fluid into a patient's prostate, or may be preferably injected deeply into the prostate tissue through a needle that is positioned transurethrally, such as in the procedure known as transurethral ethanol ablation of the prostate (TEAP); the terms "ablate, ablation, or ablating means causing a decrease in the number of tissue cells (paras. 0043-0044). Escandon et al. state that the total amount of ethanol injected will depend on a variety of factors, including, but not limited to, the size and shape of the prostate

and the nature and degree of the prostate disease (para. 0055). Escandon et al. disclose that a number of methodologies can be used to estimate prostate volume, including magnetic resonance imaging (MRI), transrectal ultrasonography (TRUS), digital rectal examination (DRE). See para. 0055. Escandon et al. teach that optionally, the chemoablation fluid to be injected may be combined with an additional additive that enhances delivery or distribution of the chemoablation fluid within the prostate tissue, or that enhances the efficacy of the chemoablation fluid (para. 0062). Escandon et al. teach that said additive can be added to the chemoablation fluid to form an injectable gel, for example, a medical-grade gelling agent such as Gelfoam Sterile Powder, which is a gelatin powder (para. 0063). Escandon et al. teach suitable alternative chemoablation agents include toxins, concentrated saline solution, other alcohols (e.g. phenol). See paras. 0066-0068. Escandon et al. teach that methods of necrosing hyperplastic prostate tissue may be conducted by a variety of surgical and non-surgical techniques, including irradiation (e.g. with microwave energy, radiofrequency, ultrasound, nuclear radiation, x-rays, or laser ablation), chemical ablation, application of heat (= thermal ablation), freezing the tissue (cryoablation). Escandon et al. state that a medication that induces damage to prostate may be utilized, wherein said medication is delivered orally, intravenously, systemically, transcutaneously or by other suitable delivery mechanisms (para. 0102). Escandon et al. teach embodiments wherein an additive is added to the chemoablation fluid to form an injectable gel e.g. a gelling agent such as GELFOAM Sterile Powder (Pharmacia & Upjohn, Kalamazoo, Mich.; para. 0063); GELFOAM is a gelatin powder consisting of particles in the 40-60 micron size

range and is commonly used as an embolizing agent (para. 0063). In addition, Escandon et al. state that an additive for enhancing visibility of the chemoablation fluid may be incorporated in the ablation fluid e.g. **the additive may comprise a dye for enhancing visualization of the chemoablation fluid during injection** (paras. 0063-0064). Escandon et al. state that better visualization of the chemoablation fluid may assist some surgeons to more effectively deliver the chemoablation fluid to the prostate tissue and to avoid undesirable backflow, wherein the dye may include methylene blue, indigo carmine, india ink, malachite green, indocyanine green, and toluidine blue (para. 0064). Also, Escandon et al. teach **alternative ablation agents**, including a suitable alcohol and phenol (carbolic acid) has been injected prostatically to ablate prostate tissue as a treatment for BPH (para. 0067). Escandon et al. disclose that a sterile aqueous mixture of phenol, glacial acetic acid, and glycerine is known in the art (para. 0067).

However, Escandon et al. do not exemplify applicant's claimed invention wherein the chemical ablation agent and biodisintegrable viscosity adjusting agent are present in a sterile injectable formulation as claimed.

It would have been obvious to a person of skill in the art at the time the invention was made to prepare a sterile injectable ablation formulation comprising ethanol (= chemical ablation agent) and Gelfoam (= biodisintegrable viscosity adjusting agent) for use in chemically ablating prostatic tissue (para. 0063). One would have been motivated to do so because Escandon et al. teach chemoablation fluids that may comprise ethanol

and Gelfoam sterile powder for injection for use in the ablation fluid of prostatic tissue and therefore one would reasonably expect to prepare said ablation fluid as a sterile injectable formulation since Escandon et al. suggest that injectable formulation can be prepared as a sterile aqueous chemoablation formulation as evidenced by the disclosure that a chemoablation formulation comprising a mixture of phenol, glacial acetic acid, and glycerine is known in the art (para. 0067). Besides, it is routine in the medical art to prepare injectable formulations that are intended to be injected into the human body in a sterile form to ensure that injectable formulations are free of microorganisms upon injection into said human body to prevent unintended microbial infections following the injection of said formulations in a human.

Regarding the term "a chemical ablation agent in an amount effective to cause necrosis" as recited in claim 1, Escandon et al. teach chemoablation gel compositions comprising a chemoablation agent (e.g. ethanol = component "a"; 0063) and therefore one would reasonably expect that the ethanol would be present in an amount effective to cause tissue necrosis. Besides, Escandon et al. teach a method of chemically ablating prostate tissue comprising injecting an effective amount ethanol or an injectable gel comprising ethanol into prostate tissue (paras. 0031-0037; see also reference claim 6).

Regarding the term "a biodisintegrable viscosity adjusting agent in an amount effective to render the formulation highly viscous" as recited in claim 1, Escandon et al. teach chemoablation gel compositions comprising a gelling agent, Gelfoam (para.

0063). Since Gelfoam is a gelling agent one would reasonably expect that the presence of Gelfoam in the composition would render the composition viscous. Further, GELFOAM is a gelatin powder and therefore reads on the term "a biodisintegrable viscosity adjusting agent in an amount effective to render the formulation highly viscous" because one would reasonably expect that gelatin would disintegrate (= biodisintegrable) following its injection into the body. That Gelfoam is a gelling agent one would reasonably expect that chemoablation fluids comprising Gelfoam would be rendered highly viscous because gels are known in the art to be highly viscous when compared to conventional liquid formulations.

With respect to the term "wherein said injectable ablation agent is a sterile injectable formulation," one would reasonably expect to formulate the chemoablation injectable gel formulation of Escandon et al. in a sterile injectable formulation since it is routine in the art to prepare sterile formulations that are intended to be injected into the human body and Escandon et al. teach a chemoablation injectable gel formulation that is also intended to be injected in the prostatic tissue of a human.

Regarding claim 2, Escandon et al. teach suitable alternative chemoablation agents including concentrated saline solution (paras. 0066-0068), which is identical to applicant's claimed osmotic-stress generating agent.

Regarding claims 3-4, Escandon et al. teach ethanol as an ablation agent and ethanol is an organic compound (paras. 0031-0037; see also reference claim 6)

Regarding claims 5-6, the above discussion of claim 2 is incorporated by reference.

Regarding claims 11-12, Escandon et al. teach that additives can be added to the chemoablation fluid to form an injectable gel, for example, a medical-grade gelling agent such as Gelfoam Sterile Powder (para. 0063), which reads on the term "wherein said viscosity adjusting agent comprises a polypeptide" as recited in claim 11 and the term "wherein said viscosity adjusting agent is selected from gelatin and collagen" as recited in claim 12 since Gelfoam is a gelatin powder.

Regarding claim 20, it would have been obvious to a person of skill in the art at the time the invention was made to prepare an injectable formulation comprising a plurality of ablation agents for additive therapeutic effects. One would have been motivated to do so because Escandon et al. suggest that a variety of surgical and non-surgical necrosing methods may be used to induce necrosis of hyperplastic prostate tissue (para. 0093) such that one would reasonably expect to successfully combine a plurality of chemoablation agents (e.g. ethanol and hypertonic saline) to the injectable formulation of Escandon et al. absent objective evidence to the contrary.

Regarding claim 21, Escandon et al. disclose that an aqueous ablation formulation comprising phenol, glacial acetic acid, and glycerine is known in the art (para. 0067) such that one would reasonably expect to add any suitable solvent (e.g. water) to the composition of Escandon et al. to solubilize the active components in the

formulation depending on the solubility of the specific components employed in the formulation.

Claims 9-10, 13, 19, are rejected under 103(a) as being unpatentable over Escandon et al. (US Patent Application Pub. No. 2003/0092689), in view of Ramsack et al. (US Patent 6,667,061)

The above discussion of Escandon et al. is incorporated by reference. This reference is silent regarding the specific instantly claimed viscosity adjusting agents and the instant claimed viscosity limitations.

Ramsack et al. teach injectable compositions, including injectable suspension, having improved injectability (col. 1, lines 17-25). Ramsack et al. teach that conventional parenteral suspensions are dilute, with limitations for viscosity because of syringeability and injectability constraints (col. 2, lines 36-39). In particular, Ramsack et al . teach comprising an aqueous injection vehicle that consists of 3% by volume sodium carboxymethyl cellulose, 1% polysorbate 20, and 0.9% sodium chloride, and a remaining percentage by volume water (col. 3, lines 1-17). Ramsack et al. teach that the composition may also comprise a viscosity enhancing agent (col. 3, lines 13-49). Ramsack et al. state that injectability is improved by increasing the viscosity of the fluid phase of an injectable suspension (col. 4, lines 57-62), which is in contrast to the conventional teachings that an increase in viscosity hinders injectability and syringeability (col. 4, lines 57-62). Ramsack et al. teach **viscosity enhancing agents** such as sodium carboxymethyl cellulose (CMC), preferably having a viscosity of from

about 1000 to about 2000 cp at 20 degrees Centigrade (col. 12, lines 13-21), but may also include, polyvinylpyrrolidone (PVP e.g. Plasdone), hydroxypropylmethylcellulose (HPMC e.g. Methocel). See col. 13, lines 41-60). Ramsack et al. teach wetting agents such as polysorbate 20 (Tween 20), polysorbate 40 (Tween 40), and polysorbate 80 (Tween 80; col. 16, lines 1)

It would have been obvious to a person of skill in the art at the time the invention was made to combine the teachings of the cited references by adding any suitable biodisintegrable viscosity adjusting agent as taught by Ramsack et al. (e.g. sodium carboxymethyl cellulose) or a plurality of said agents to improve the syringeability and injectability of the formulation. One would have been motivated to do so because Ramsack et al. suggest that increasing the viscosity of injectable formulations with the use of viscosity enhancing agents (e.g. carboxymethyl cellulose) improves the syringeability and injectability of injectable formulations (col. 4, lines 63-67; col. 6, lines 9-19; and col. 7, lines 37-39; and col. 12, lines 13-16) and Escandon et al. teach that optionally, the chemoablation fluid to be injected may be combined with an additional additive that enhances delivery or distribution of the chemoablation fluid within the prostate tissue, or that enhances the efficacy of the chemoablation fluid (para. 0062).

Further, it would have been obvious to a person of skill in the art at the time the invention was made to manipulate the viscosity of the formulation by using a viscosity enhancing agent, including arriving at applicant's claimed viscosity range, to optimize the injectability and syringeability of the ablation formulation. One would have been

motivated to do so because Ramsack et al. suggest injectable compositions comprising viscosity enhancing agents wherein the viscosity is at least 20 cps have good syringeability and injectability and Escandon et al. teach injectable gel formulations comprising gelfoam which also enhance the viscosity of the formulation. Hence, one would reasonably expect to successfully manipulate the viscosity of the formulation of Escandon et al. to arrive at the instant claimed viscosity limitations since Ramsack et al. suggest that increasing the viscosity of injectable formulations improve the syringeability and injectability of injectable formulation absent objective evidence to the contrary.

Regarding claims 9-10, Ramsack et al. teach sodium carboxymethyl cellulose (col. 3, lines 1-17), which reads on the term "wherein said viscosity adjusting agent comprises a polysaccharide" as recited in claim 9 and the term "carboxymethyl cellulose and its salts" as recited in claim 10.

Regarding claim 13, Ramsack et al. teach preferred viscosity enhancing agents, including polyvinylpyrroildone (PVP; col. 13, lines 13-22), which overlap with the instant claimed viscosity adjusting agents.

Regarding claim 19 , it would have been obvious to a person of skill in the art at the time the invention was made to use any suitable viscosity enhancing agent(s) as taught by Ramsack et al. to the chemoablation fluid of Escandon et al., including using a plurality of viscosity adjusting agents as claimed, depending on the desired characteristics of the formulation. One would have been motivated to do so because

Ramsack et al. suggest that syringeability and injectability of injectable formulations can be varied by the use of viscosity enhancing agents (col. 4, lines 63-67; col. 6, lines 9-19; and col. 7, lines 37-39; and col. 12, lines 13-16) and Escandon et al. teach formulations that may comprise a gelling agent and therefore one would reasonably expect to manipulate the number of viscosity enhancing agents used in the formulation encompassed to optimize the syringeability and injectability of the chemoablation formulation encompassed by the prior art absent objective evidence to the contrary.

Thus, one would have deemed it obvious to create the instant claimed invention with reasonable predictability.

Claims 7-8 are rejected under 103(a) as being unpatentable over Escandon et al. (US Patent Application Pub. No. 2003/0092689), in view of Ramsack et al. (US Patent 6,667,061), in further view of Lund (US Patent 3,869,546).

The above discussions of Escandon et al. and Ramsack et al. are incorporated by reference. These references do not teach the instant claimed viscosity ranges.

Lund teach improved injectable mixtures containing biologics, a polymer, and an electrolyte having a viscosity of about 500 to about 50,000 cps, depending on the relative concentration of the polymer (col. 6, lines 36-46). Lund state that the viscosity of polymer-electrolyte adjuvant solutions should generally be about several hundred to a few thousand centipoise for ease of passing through hypodermic needles (col. 4, lines 39-42).

It would have been obvious to a person of skill in the art at the time the invention was made to combine the teachings of the cited references to manipulate the viscosity of the ablation formulation encompassed by the prior art to optimize the injectability of the formulation. One would have been motivated to do so because Lund suggest that the viscosity of formulations that are injected via hypodermic needles should be about 500 to about 50,000 cps, depending on the relative concentration of the polymer (col. 6, lines 36-46) and Ramsack et al. also state that injectability is improved by increasing the viscosity of the fluid phase of an injectable suspension (col. 4, lines 57-62). Hence, one would reasonably expect to successfully manipulate the viscosity of the formulation of Escandon et al. in order to enhance its injectability because Escandon et al. teach formulations for injection.

It is noted that the viscosity range taught by Lund overlaps with the instant claimed viscosity ranges recited in claims 7 and 8.

Thus, one would have deemed it obvious to create the instant claimed invention with reasonable predictability.

Claims 14, 16-18 are rejected under 103(a) as being unpatentable over Escandon et al. (US Patent Application Pub. No. 2003/0092689), in view of Glajch et al. (US Patent 5,147,631; already made of record).

The above discussion of Escandon et al. is incorporated by reference. Escandon et al. do not teach solid imaging particles or ultrasound contrast agents.

Glajch et al. teach **ultrasound contrast agents comprising porous particles** of an inorganic material having an average particle diameter of about 0.05 to 500 microns and containing entrapped gas or liquid; the inorganic material includes monomeric and polymeric forms of one or more of the following: borates, aluminas, carbonates, silicates, silicas, aluminosilicates, phosphates, and organic or inorganic cationic salts thereof (column 2, lines 11-27).

It would have been obvious to a person of skill in the art at the time the invention was made to combine the teachings of the cited references by adding any suitable solid imaging contrast agent (e.g. inorganic material comprising a monomeric or polymeric form of a silicate) to enhance the visualization of the ablation fluid. One would have been motivated to do so because Escandon et al. suggest that optionally additives can be added to the ablation fluid to enhance visualization of the ablation fluid and ultrasound contrast agents taught by Glajch et al. are used to enhance visualization of body parts. In addition, Escandon et al. disclose that a number of methodologies can be used to estimate prostate volume, including magnetic resonance imaging (MRI), transrectal ultrasonography (TRUS) and digital rectal examination (DRE; para. 0055) such that one would reasonably expect to add an ultrasonic imaging contrast agent in the form of solid particles to the chemoablation fluid to determine the prostatic volume since Escandon et al. suggest that magnetic resonance imaging (MRI), and transrectal ultrasonography (TRUS) can be used to estimate prostatic volume.

Regarding claims 14 and 16, Glajch et al. teach ultrasound contrast agents comprising porous particles (column 2, lines 11-27), which overlaps with the instant claims.

With respect to claim 17, it is noted that the term "wherein the ultrasonic imaging agent contrast agent comprises a plurality of solid particles" does not require the plurality of particles to be different from each other.

Regarding claim 18, Glajch et al. teach silicate particles (col. 2, lines 11-27).

Thus, one would have deemed it obvious to create the instant claimed invention with reasonable predictability.

Claim 15 is rejected under 103(a) as being unpatentable over Escandon et al. (US Patent Application Pub. No. 2003/0092689), in view of Lauffer et al. (US Patent 7,175,829).

The above discussion of Escandon et al. is incorporated by reference. However, this reference does not teach MRI contrast imaging agents.

Lauffer et al. (US Patent 7,175,829) teach a method for contrast-enhanced diagnostic imaging, particularly MRI, of a specific tissue or tissue component (col. 4, line 65 to col. 5, line 1). Lauffer et al. disclose that diagnostic imaging technique has been used to monitor interventional therapies, which include targeting an undesired tissue or tissue component with high thermal energy using focused **ultrasound** (col. 2, lines 4-41). Lauffer et al. state that a goal of interventional therapies is the treatment of undesirable tissue or tissue component, such as cancerous, tumorous, neoplastic tissue

or tissue component, by causing **necrosis, ablation, coagulation, or denaturation of such tissue** (col, 2, lines 37-41). To obtain the maximum benefit from such interventional methods, and to minimize side effects (e.g. damage to adjacent tissues), it is essential to monitor, in vivo, the efficacy of the therapy (col. 2, lines 42-54). Lauffer et al. teach methods comprising administering to a patient **a contrast agent capable of binding to a targeted tissue or tissue component that is undergoing or has undergone interventional therapy; wherein said patient is subjected to one of MRI**, ultraviolet light, visible light or infrared imaging; and further wherein said method involves monitoring an imaging signal characteristic of the contrast agent to determine whether the interventional therapy is completed (col. 6, lines 9-27).

It would have been obvious to a person of skill in the art at the time the invention was made to combine the teachings of the cited references to employ contrast imaging agents (e.g. MRI or ultrasound) as taught by Lauffer et al. to monitor the effect of the ablative therapy. One would have been motivated to do so because Lauffer et al. suggest that contrast imaging agents are useful to monitor the efficacy of interventional therapies such as ablative therapies (col. 2, lines 42-54) and Escandon et al. disclose that a number of methodologies can be used to estimate prostate volume, including magnetic resonance imaging (MRI; para. 0055) such that one would reasonably expect to add MRI imaging contrast agent to the ablation formulation to monitor the efficacy of the ablation therapy.

Regarding claim 15, Lauffer et al. teach MRI imaging contrast agents (col. 6, lines 9-27).

Thus, one would have deemed it obvious to create the instant claimed invention with reasonable predictability.

Claims 38-39 are rejected under 103(a) as being unpatentable over Escandon et al. (US Patent Application Pub. No. 2003/0092689), in view of Cochrum (US Patent 5,614,204).

The above discussion of Escandon et al. is incorporated by reference. However, this reference does not teach the instant claimed ionically crosslinkable polymer.

Cochrum (US Patent 5,614,204) teach angiographic occlusion agents prepared from a biocompatible polymer alone to achieve a permanent occlusion or in combination with a platelet-rich plasma concentrate to achieve a semi-permanent or temporary occlusion (col. 1, lines 8-22). Cochrum et al. exemplify sodium alginate spheres for use as a permanent angiographic vascular occlusion agent (col. 16, Example 1). Cochrum teach vascular occlusion agents for various uses, including **embolic therapy for organ ablation** (col. 15, lines 5-25). Cochrum et al. teach that selective vascular embolization has been employed to treat, for example, **acute hemorrhage vascular tumors and organ ablation** (col. 1, lines 27-31). Cochrum state that materials such as Gelfoam, and other particulate materials, are useful occlusion materials (col. 2, lines 24-26). It would have been obvious to a person of skill in the art at the time the invention was

made to combine the teachings of the cited references by adding an angiographic occlusion agent (e.g. sodium alginate spheres = ionically crosslinkabel polymer) as taught by Cochrum et al. to the injectable chemoablation formulation of Escandon et al. for additive ablative effect. One would have been motivated to do so because Cochrum et al. suggest that sodium alginate and Glefoam are useful occlusion agents for use in organ ablation therapy (col. 1, lines 27-31) and Escandon et al. state that the ablating action of the ethanol is due to several processes, including dehydration of cells, coagulation of proteins, and thrombosis of vessels that feed the tissue (para. 0044, last three lines). Since Cochrum suggest embolic occlusive agents (e.g. sodium alginate) are desirable for use in organ ablation therapy (col. 1, lines 27-31), one would reasonably expect to add an said embolic occlusive agent to the ethanol/Gelfoam formulation as taught be Escandon et al. to improve the ablative properties of the formulation.It is noted that Cochrum et al. teach sodium alginate spheres, which reads on the term "ionically crosslinkabel polymer" as recited in claim 38 and the term "an alginate polymer" as recited in claim 39.

Thus, one would have deemed it obvious to create the instant claimed invention with reasonable predictability.

Response to applicant's arguments

Applicant's arguments with respect to the rejection under 103(a) claim has been considered but are moot in view of the new ground(s) of rejection.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charlesworth Rae whose telephone number is 571-272-6029. The examiner can normally be reached between 9 a.m. to 5:30 p.m. Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila G. Landau, can be reached at 571-272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http:pair-direct.uspto.gov. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 800-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

1 June 2009
/C. R./
Examiner, Art Unit 1611

/Sharmila Gollamudi Landau/

Supervisory Patent Examiner, Art Unit 1611